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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/685,823	10/09/2000	Ellen H. Filvaroff	P1834	4430

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EXAMINER	
JIANG, DONG	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 09/26/2002

13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/685,823	FILVAROFF, ELLEN H.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 July 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-9,21,23-29,37 and 39-46* is/are pending in the application.

4a) Of the above claim(s) *41-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-9,21,23-29,37,39,40,45 and 46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1,3-9,21,23-29,37 and 39-46* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED OFFICE ACTION

Applicant's amendment in paper No. 12, filed on 08 July 2002 is acknowledged and entered. Following the amendment, claims 16-20 are canceled, and claims 1, 9, 29 and 37 are amended.

Currently claims 1, 3-9, 21, 23-29, 37, 39-46 are pending, and claims 1, 3-9, 21, 23-29, 37, 39, 40, 45 and 46 are under consideration.

Withdrawal of Objections and Rejections:

All objections and rejections of claims 16-20 are moot as the applicant has canceled the claims.

The rejection of claims 9 and 29 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn in view of applicant's amendments.

The scope rejection of claims 1, 3-5, 8, 9, 21, 23-25, 28, 29, 37, 39, 40 under 35 U.S.C. 112, first paragraph is withdrawn in view of applicant's argument.

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 3-6, 8, 9, 21-26, 28, 29, 37, 39, 40, and 45 remain rejected under 35 U.S.C. 102(a) as being anticipated by Shigeru et al., JP2000186046 (July 4, 2000) for the reasons cited in the previous Office Action, paper No. 6, at page 6.

Applicants argument, filed on 08 July 2002 (paper No. 12) has been fully considered, but is not deemed persuasive for reasons below.

At page 5 of the response, the applicant argues that Shigeru discloses that anti-IL-17 can inhibit osteoclastrogenesis induction by IL-17, thus might be useful in treating RA, but not OA, trauma or gout, as IL-17 was found in RA patients, but not those with other disoreders. This

argument is not persuasive because regardless whether there is a difference between RA and OA, so long as Shigeru's teaching, a method of treating RA with anti-IL-17 antibody, meets the limitation of the claims, the Shigeru reference anticipates the claims.

The applicant further argues that Shigeru does not recognize that IL-17 has a deleterious effect on cartilage, and anti-IL-17 can treat further damage to cartilage caused by IL-17, and that the present claims are specified to the treatment of cartilage. This argument is not persuasive because, again, it is irrelevant whether Shigeru recognizes the exact pathological effect or mechanism of IL-17 at the cellular or molecular levels, so long as Shigeru's teaching meets the limitation of the claims, which are drawn to a method of treating an IL-17 mediated cartilaginous disorder with an anti-IL-17 antibody, the Shigeru reference anticipates the claims as Shigeru teaches a method of treating RA using an IL-17 neutralizing antibody. Additionally, as Shigeru's method steps are the same as those in the present claims, the therapeutic effect of the treatment on cartilage is inherent.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-6, 8, 9, 21, 23-26, 28, 29, 37, 39, 40, and 45 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Chabaud et al. (J. Immunol., 1998, 161:409-414), in view of Carroll et al. (Inflammation Research, 47:1-7, 1998) for the reasons cited in the previous Office Action, paper No. 6, at pages 7-8.

Applicants argument in paper No. 12 has been fully considered, but is not deemed persuasive for reasons below.

At page 6 of the response, the applicant argues that the combined teachings of the references fail to recognize that a common cytokine can treat cartilage damaged from both rheumatoid- and osteo-arthritic causes. This argument is not persuasive because nowhere in the claims the treatment of *both* rheumatoid- and osteo-arthritic causes is required, and all that is

required in the claims is to treat *a* cartilaginous disorder. Additionally, applicant's attention is directed to the fact that only those claims in which the limitation is generic or specifically directed to RA, are rejected under this rejection. The applicant further argues that the prior art establishes that IL-17 can induce the production of IL-6, however, the claimed method relates to the use of anti-IL-17 antibodies for the treatment of cartilage in IL-17 mediated inflammatory disorders, not those mediated by IL-6, thus the inhibition of the downstream IL-6 will not necessarily inhibit the same spectrum of disorders as the inhibition of IL-17, and combined teaching does not teach the inhibition of IL-17 by an anti-IL-17 is effective for damaged cartilage. This argument is not persuasive because, while the Examiner agrees that the inhibition of the downstream IL-6 may not inhibit the same spectrum of disorders as the inhibition of IL-17, the teaching by Chabaud is to use a blocking anti-IL-17 antibody, *not* the inhibition of IL-6. The reduced production of IL-6 was only the consequence of using blocking *anti-IL-17* antibody observed by Chabaud. Additionally, the effectiveness for damaged cartilage is irrelevant because an effect is intended result, and does not result in a manipulative difference in the method itself, and it is inherently same from the methods comprising the same steps.

At page 7 of the response, the applicant further argues that combined teaching does not teach that anti-IL-17 or even anti-IL-6 antibodies might be useful to treat further damage to *cartilage*, and does not recognize that the attenuation of IL-17 would be effective in specifically treating cartilage damage. This argument is not persuasive because it is well established in the art that cartilage is a part of the joint tissue, and the involvement of cartilage in arthritis is well known. While the prior art is directed to arthritis of joints, the cartilage is included. As the applicant points out, the Examiner is aware the complex pathology of arthritis, however, given the feature of the anatomical structure of a joint, it is unclear how one is capable of treating the cartilage exclusively while applying anti-IL-17 antibody to the joint with the disease. Therefore, even though the references are silent about treating cartilage, they still render the present claims obvious because the teachings are directed to arthritis, which is a cartilaginous disorder. Additionally, the cited references are used to reject the claims under 35 U.S.C. 103(a), that is to render the claims obvious, *not to anticipate* the claims. Therefore, even though neither reference teaches exactly the treatment of an arthritis patient with anti-IL-17 antibody, together they clearly suggest such. For instance, as cited in the previous Office Action, Chabaud teaches that

"production of biologically active IL-17 was demonstrated in RA synovium supernatants", "RA synovium T cells producing IL-17 can activate mesenchymal cells leading to an increased proinflammatory pattern", and a blocking anti-IL-17 antibody reduced production of IL-6 and LIF, which are mediators of inflammation, and that "control of the production and action of IL-17 may represent a therapeutic target for reducing the enhancing effect of monocyte-derived cytokines". Based on the teaching and suggestion by the prior art, the person of skill in the art would immediately envision that inhibition of IL-17 with anti-IL-17 would reasonably be expected to therapeutic value in treatment of RA.

Claims 1-4, 8-9, 13, 14, 21-26, 28, 29, 33, 34, 37-39 and 45 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Kotake et al. (J. Clin. Invest., 1999, 103:1345-1352), and Chabaud et al. (Arthritis & Rheumatism, 1999, 42:963-970), in view of Carroll et al. (Inflammation Research, 47:1-7, 1998) for the reasons cited in the previous Office Action, paper No. 6, at page 8, and reasons above and below.

Applicants argument in paper No. 12 has been fully considered, but is not deemed persuasive for reasons below.

At page 8 of the response, the applicant argues that Kotake describes that the use of anti-IL-17 antibody to prevent osteoclast formation, and cartilage is not even mentioned in the reference, therefore, no suggestion or motivation either in Kotake or the combined teaching of the three references to use a treatment for decreasing bone growth as a treatment for damage to cartilage. This argument is not persuasive because Kotake's study is directed to RA and OA, and the reported effect of anti-IL-17 antibody to prevent osteoclast formation is associated with the diseases. Osteoclastic bone resorption is merely a part of the pathological changes of RA (the abstract), and it is well known that the disease involves multiple pathological changes, including cartilage damage. Therefore, treating osteoclastic bone resorption of RA with anti-IL-17 antibody would have the inherent effect on cartilage damage of RA even though Kotake is silent about the effect on cartilage damage.

Claims 1, 3-9, 21, 23-29, 37, 39, 40, 45, and 46 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Troutt (WO 98/23284), in view of Chabaud et al. (J. Immunol., 1998, 161:409-414), for the reasons cited in the last Office Action, paper No. 10, at pages 6-7.

Note, the Chabaud reference was mis-cited as "Carroll et al. (Inflammation Research, 47:1-7, 1998)" in the previous Office Action, as the quoted teachings in the rejection are from Chabaud, not Carroll.

Applicants argument in paper No. 12 has been fully considered, but is not deemed persuasive for reasons below.

At pages 8-9 of the response, the applicant argues that Troutt teaches that IL-17 upregulated the release of NO, and that inhibitors of IL-17 will be useful in regulating levels of NO, and will find therapeutic application in ameliorating the effects of NO in OA, as well as autoimmune and inflammatory diseases, however, Example 1D and Figure 5 in the instant specification suggest that NO could actually have an overall beneficial effect. The applicant further argues that while Troutt demonstrates that the antagonism of IL-17 attenuates NO production, it does not take the next step of suggesting the attenuation of NO is effective in treating further damaging to cartilage, and without the hard experimental data, a theory remains just that, a theory. The applicant further argues that the combined teaching does not teach or suggest that anti-IL-17 antibody might be useful to treat cartilage damage from a disease state. This argument is not persuasive because it is irrelevant whether Troutt's theory is correct or not, as the applicant states that it is just a theory, and it does not results in a manipulative difference in the method of treatment itself, even if Troutt's theory or proposed mechanism of inhibition of IL-17 in RA and OA patients is incorrect. The key issue is that Troutt teaches a method of treating OA and RA by administering an *IL-17 inhibitor*. As Chabaud teaches that an anti-IL-17 antibody can antagonize IL-17 by demonstrating the blocking effect of IL-17 on the production of IL-6 and LIF, it becomes clear that such an antibody is an IL-17 inhibitor. Therefore, based on the combined teaching by Troutt and Chabaud, the person of skill in the art would immediately envision that an anti-IL-17 antibody can be used to substitute the soluble IL-17R in Troutt's method to achieve the similar effect, that is to antagonize IL-17. With respect to the

argument of treating cartilage damage, as Troutt's method is directed to the treatment of OA or RA, which are cartilaginous disorders, the effect on cartilage damage using the same method is inherent.

Conclusion: No claim is allowed.

Advisory Information:

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 703-305-1345. The examiner can normally be reached on Monday - Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER

DJ
9/9/02